

Applicants: Yuti Chernajovsky et al.
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Filed: April 2, 1999
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Please amend the subject application as follows:

Amendment to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims:

1.-13. (Cancelled)

14. (Currently Amended) An The isolated DNA of Claim 8 encoding a receptor molecule which binds to tumor necrosis factor comprising all or a functional portion of two or more extracellular domains of tumor necrosis factor receptors linked to a polypeptide linker, wherein said polypeptide linker is from about 10 to about 30 amino acid residues in length and is covalently bonded to said extracellular domains via peptide bonds, wherein the receptor molecule is capable of binding to a tumor necrosis factor trimer in a stoichiometric ratio of almost 1:1, and wherein the DNA comprises the nucleic acid sequence set forth in SEQ ID NO:1.

15.-27. (Cancelled)

28. (Currently Amended) An The isolated DNA of claim 8 encoding a receptor molecule which binds to tumor necrosis factor comprising all or a functional portion of two or more extracellular domains of

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tumor necrosis factor receptors linked to a polypeptide linker, wherein said polypeptide linker is from about 10 to about 30 amino acid residues in length and is covalently bonded to said extracellular domains via peptide bonds, wherein the receptor molecule is capable of binding to a tumor necrosis factor trimer in a stoichiometric ratio of almost 1:1, and wherein the polypeptide comprises consecutive amino acids having the amino acid sequence set forth in SEQ ID NO:2.

29. (Previously Presented) A receptor molecule which binds to tumor necrosis factor comprising all or a functional portion of two extracellular domains of tumor necrosis factor receptors linked to a polypeptide linker, wherein the molecule comprises the amino acid sequence of SEQ ID NO:2.

30. (Previously Presented) A method of making a construct which expresses all or a functional portion of the extracellular domain of two or more tumor necrosis factor receptors linked to a polypeptide linker wherein the construct expresses the amino acid sequence of SEQ ID NO:2, comprising the steps of:

- a) obtaining a first vector which expresses all or a functional portion of an extracellular domain of a first tumor necrosis factor receptor and a signal peptide of a secreted protein;

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- b) obtaining a second vector which expresses all or a functional portion of an extracellular domain of a second tumor necrosis factor receptor; and
 - c) ligating the first vector of (a) to the second vector of (b) using a coding sequence for a polypeptide linker so that the first vector of (a) is linked to the second vector of (b) using the coding sequence for the polypeptide linker resulting in a construct which expresses all or a functional portion of the extracellular domain of the first tumor necrosis factor receptor and all or a portion of the extracellular domain of the second tumor necrosis factor receptor linked using the polypeptide linker.
31. (Previously Presented) A method of making a construct which expresses all or a functional portion of the extracellular domain of more than two tumor necrosis factor receptors linked to a polypeptide linker where the construct expresses the amino acid sequence set forth in SEQ ID NO:2, comprising the steps of:
- a) obtaining a first vector which codes for all or a functional portion of an extracellular domain of a first tumor necrosis factor receptor and signal

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peptide of a secreted protein linked to all or a functional portion of an extracellular domain of a second tumor necrosis factor receptor using a coding sequence for a polypeptide linker;

- b) obtaining a second vector which codes for all or a functional portion of an extracellular domain of a third tumor necrosis factor receptor; and
- c) ligating the first vector of (a) to the second vector of (b) using a coding sequence for a polypeptide linker so that the first vector of (a) is linked to the second vector of (b) using the coding sequence for a polypeptide linker resulting in a construct which expresses all or a functional portion of the extracellular domain of the first tumor necrosis factor receptor and all or a portion of the extracellular domain of the second tumor necrosis factor receptor and all or a portion of the extracellular domain of the third tumor necrosis factor receptor all being linked using the first and second polypeptide linkers.

32. (Previously Presented) A cell which expresses a receptor molecule encoded by the DNA of Claim 28.

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33. (Previously Presented) A method of inhibiting the biological activity of tumor necrosis factor comprising administering to a subject a TNF-inhibiting amount of a receptor molecule encoded by the DNA of Claim 28.
34. (Previously Presented) A method of treating a tumor necrosis factor-related disease in a subject in need thereof comprising administering to the subject a tumor necrosis factor-inhibiting amount of a receptor molecule encoded by the DNA of Claim 28.
35. (Previously Presented) The method of Claim 34, wherein the tumor necrosis factor-related disease is selected from the group consisting of: an autoimmune disease, an inflammatory bowel disease, a bacterial infection, a viral infection, a parasitic infection, a malignancy, and a neurodegenerative disease.
36. (Previously Presented) The method of Claim 35, wherein the tumor necrosis factor-related disease is selected from the group consisting of: rheumatoid arthritis, septic shock, cerebral malaria, inflammatory bowel disease, multiple sclerosis, allograft rejection, host versus graft disease, neoplastic pathology and endotoxemic response.

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37. (Previously Presented) The method of Claim 34, wherein the tumor necrosis factor-related disease is rheumatoid arthritis.